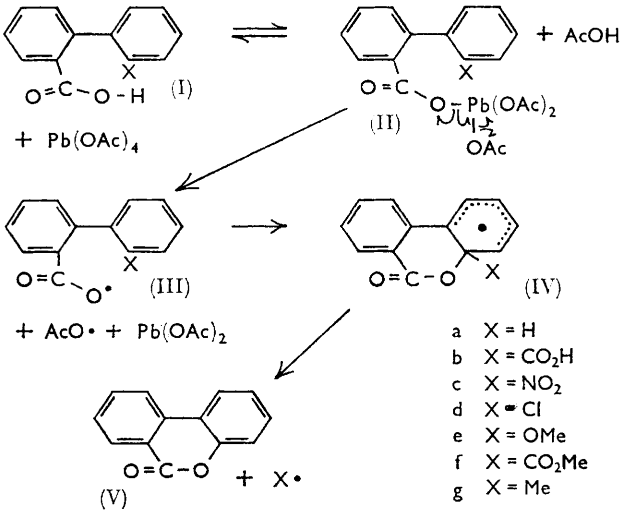
Cyclisation Reactions Involving the Oxidation of Carboxylic Acids with Lead Tetra-acetate. Part I. The Conversion of 2′-Substituted Biphenyl-2-carboxylic Acids into 3,4-Benzocoumarin

By **D. I. Davies*** and **C. Waring**, Department of Chemistry, King's College, Strand, London W.C.2

The reaction of 2′-substituted biphenyl-2-carboxylic acids (where the 2′-substituent is H, CO_2H, NO_2, Cl, OMe, or CO_2Me) with lead tetra-acetate in refluxing benzene solution, under a nitrogen atmosphere, affords 3,4-benzocoumarin as a major organic product. Only a trace is formed when the 2′-substituent is Me. *o*-Terphenyl-2-carboxylic acid gives no 3,4-benzocoumarin, but triphenylene is formed in good yield. It is suggested that these cyclizations involve the intermediacy of free radicals, particularly as the products of the thermal decomposition, in benzene solution, of the diacyl peroxides derived from 2′-substituted biphenyl-2-carboxylic acids, are similar to the products formed on reaction of the acids with lead tetra-acetate.

The most recent studies on the reaction of lead tetra-acetate with carboxylic acids [1-5] (acids belonging to the norbornane [6] and the bornane [7] series may be exceptions) indicate that the organic products are derived from free-radical intermediates. A study of the reaction of the 2′-substituted biphenyl-2-carboxylic acids (Ia)—(Ig) with lead tetra-acetate in boiling benzene, under a nitrogen atmosphere, has shown that with the exception of the methyl-acid (Ig), 3,4-benzocoumarin (V) is a major product in each case (see Table). The most likely mechanism for the formation of 3,4-benzocoumarin (V) is therefore *via* the intermediates (II), (III), and (IV), and involves a free-radical displacement of the substituent group in the final steps (III) ⟶ (IV) ⟶ (V). In the oxidation of 2′-chlorobiphenyl-2-carboxylic acid (Id), 2-chloro-*o*-terphenyl and *o*-chlorobiphenyl are additional reaction products. They provide evidence for the intermediacy of free radicals in that their formation is most satisfactorily explained *via* 2′-chlorobiphenyl-2-yl radicals, which either substitute in the solvent benzene or abstract hydrogen from a suitable donor. Competition between the intramolecular substitution reaction (IIId) ⟶ (IVd) ⟶ (V) and decarboxylation to 2′-chlorobiphenyl-2-yl radicals is readily suggested. 2-Methoxycarbonyl-*o*-terphenyl is likewise an additional product produced from the methoxycarbonyl-acid (If), but similar products are not formed from the other acids, which indicates that the ease of the displacement of the group X relative to decarboxylation is dependent on the nature of the group X. The thermal decomposition, in benzene solution, of diacyl peroxides,[8] even if highly asymmetrical,[9] invariably proceeds by a free-radical pathway. Further support for the importance of free-radical intermediates in product formation from the lead tetra-acetate oxidation of the acids (I) is therefore provided by the observation that the products from thermal decomposition of the diacyl peroxides derived from the acids (Ia),[10-13] (Ic), and (Id) are the same as those formed on the lead tetra-acetate oxidation of these acids. We could not prepare a diacyl peroxide of the methoxy-acid (Ie).



The acid chloride is required as an intermediate in the preparation of the peroxide, but, like Rule and Bretscher [14] we found that the acid (Ie) is converted to 3,4-benzocoumarin (V) on reaction with thionyl chloride or phosphorus halides. Therefore, the possibility of an ionic mechanism involving the cleavage of the O–Me bond cannot be ruled out.† We prefer, however, analogy to the reaction of the methoxy-acid (Ie) with persulphate in which 3,4-benzocoumarin [15] is formed by a free-radical process.[16] The carboxylate anion

---

† We are grateful to the referees for this suggestion.

[1] D. I. Davies and C. Waring, *Chem. Comm.*, 1965, 263.

[2] J. K. Kochi, *J. Amer. Chem. Soc.*, 1965, **87**, 1811.

[3] J. K. Kochi, *J. Amer. Chem. Soc.*, 1965, **87**, 3609.

[4] J. K. Kochi, *J. Amer. Chem. Soc.*, 1965, **87**, 2500.

[5] T. W. Bethea and J. K. Kochi, American Chemical Society, Abstracts of 150th Meeting, page 12 S.

[6] E. J. Corey and J. Casanova, jun., *J. Amer. Chem. Soc.*, 1963, **85**, 165.

[7] G. E. Gream and D. Wege, *Tetrahedron Letters*, 1967, 503.

[8] G. H. Williams, "Homolytic Aromatic Substitution," Pergamon Press, London, 1960.

[9] J. E. Leffler, *J. Amer. Chem. Soc.*, 1950, **72**, 67.

[10] G. W. Kenner, M. A. Murray, and C. M. B. Taylor, *Tetrahedron*, 1959, **1**, 259.

[11] J. K. Kochi and R. D. Gilliom, *J. Amer. Chem. Soc.*, 1964, **86**, 5251.

[12] F. D. Greene, G. R. van Norman, J. C. Cantrill, and R. D. Gilliom, *J. Org. Chem.*, 1960, **25**, 1790.

[13] D. B. Denney and P. P. Klemchuk, *J. Amer. Chem. Soc.*, 1958, **80**, 3289.

[14] H. G. Rule and E. Bretscher, *J. Chem. Soc.*, 1927, 925.

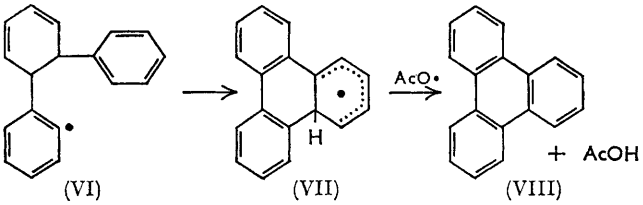
[15] J. Russell, R. H. Thomson, and A. G. Wylie, *Chem. and Ind.*, 1964, 34.

[16] J. Russell and R. H. Thomson, *J. Chem. Soc.*, 1962, 3379.

of the nitro-acid (Ic) can displace the nitro-group to give 3,4-benzocoumarin,[17] but this mechanistic pathway is unlikely to be followed in the lead tetra-acetate oxidation, as the displacement by carboxylate anion requires a temperature $\sim$100° higher than that employed. Likewise, we do not favour a similar carboxylate anion displacement proposed by Moore and Arzoumanian [18] as a possible mechanism for the formation of 3,4-benzocoumarin (V) on oxidation of biphenyl-2,2′-dicarboxylic acid (Ib) with lead tetra-acetate in pyridine–acetonitrile. We prefer our free radical mechanism, particularly as Kochi [3] has shown that pyridine does not affect the free-radical nature of the lead tetra-acetate oxidations. In the oxidation of the methyl-acid (If) only a trace of 3,4-benzocoumarin is produced, which reflects both the difficulty of displacement of the methyl group, and its potential ease of oxidation.[19,20]

A search for products derived from the displaced group revealed traces of nitrobenzene and anisole from the nitro- and methoxy-acids (Ic) and (Ie), respectively. Appreciable chloride ion is produced from the chloro-acid (Id), but we failed to detect any formaldehyde (the potential product of proton loss from a methoxy-cation) from the methoxy-acid (Ie) or nitrogen dioxide from the nitro-acid (Ic). In the oxidising medium of the reactions, the possibility of a displaced group becoming an ion cannot be overlooked, and therefore it is not possible to make meaningful deductions based on the products derived from the displaced group.

o-Terphenyl-2-carboxylic acid (I; X = Ph) on reaction with lead tetra-acetate gave no 3,4-benzocoumarin (V), which would arise from an intramolecular displacement of the phenyl group. Triphenylene (VII) was formed in quantitative yield and we suggest that the *o*-terphenyl-2-carboxy-radical (III; X = Ph) loses carbon dioxide to give the *o*-terphenyl-2-yl radical (VI) from which triphenylene is formed in an intramolecular process (VI) ⟶ (VII) ⟶ (VIII). Thermal decomposition of the diacyl peroxide of *o*-terphenyl-2-carboxylic acid similarly produces triphenylene (VIII).[21]



(VI) (VII) (VIII)

Among the products of the lead tetra-acetate oxidation of the acids (Ib), (Ic), and (Id) is some biphenyl. Biphenyl is not a product of the reaction of lead tetra-acetate with benzene,[22] but it may arise by the abstraction of hydrogen from the solvent benzene, by one of the various free radicals produced in the reaction, to form a phenyl radical. This would produce biphenyl by substitution in the solvent. We cannot put forward a credible process by which biphenyl may be derived from these acids by loss of both the 2′-substituent and the carboxy-groups.

The reaction times varied greatly with the 2′-substituent. Both the nitro- and the methyl-acids (Ic) and (Ig) were slow to react. This is perhaps surprising in view of the opposite electrical characteristics of these groups. However, the interaction of the 2′-substituent with the carboxy-group may well be considerable in the case of these two acids due to hydrogen bonding between the methyl group and the carboxy-carbonyl, and to attraction between the positively charged nitrogen of the nitro-group and the carboxy-carbonyl. This would retard the first stage of the reaction involving ionic interchange between the acids and lead tetra-acetate to give intermediates of type (II).

EXPERIMENTAL

The n.m.r. spectra were determined using a Perkin-Elmer R.10 instrument operating at 60 Mc./sec. and the i.r. spectra using a Perkin-Elmer 237 grating i.r. spectrometer. Qualitative analytical g.l.c. was carried out using a Pye Argon Chromatograph and the following 4 ft. columns: A, 5% Apiezon L grease; B, 10% Apiezon L grease. Quantitative g.l.c. was carried out using a Griffin D6 Density Balance Chromatograph with nitrogen carrier gas and a 6 ft. column of 5% Apiezon L grease; Celite (80—100 mesh) was used as inert support. Preparative g.l.c. was carried out using a Wilkens Autoprep 700 employing hydrogen as carrier gas and a 10 ft. × $\frac{3}{8}$ in. column of 20% Apiezon L grease on 40/60 Chromosorb W. Thick-layer chromatography was performed using 8 in. square glass plates coated with " Merck " Kieselgel G.

The structures of known compounds isolated were demonstrated by m. p. and mixed m. p. determinations, and comparison of g.l.c. retention times and i.r. spectra with those of authentic specimens.

Preparation of Acids.—Biphenyl-2-carboxylic acid (Ia) biphenyl-2,2′-dicarboxylic acid (Ib) from Koch–Light were recrystallised from ethanol; m. p. 114 and 233° respectively. 2′-Nitrobiphenyl-2-carboxylic acid (Ic),[17] m. p. 170°; 2′-methoxycarbonylbiphenyl-2-carboxylic acid (If),[23] m. p. 110°; 2′-methoxybiphenyl-2-carboxylic acid (Ie),[14] m. p. 152—153°; *o*-terphenyl-2-carboxylic acid (I; X = Ph),[21] m. p. 124—126°; 2′-chlorobiphenyl-2-carboxylic acid (Id),[24] m. p. 142·5—143·5°.

2′-Methylbiphenyl-2-carboxylic acid (Ig). Copper-bronze (80 g.), *o*-iodotoluene (40 g.), and methyl *o*-iodobenzoate (40 g.) were intimately mixed and heated at 200° for 1 hr. and then at 250° for 5 hr. (The initial reaction is exothermic and care must be taken to prevent the initial

---

[17] D. H. Hey, J. A. Leonard, and C. W. Rees, *J. Chem. Soc.*, 1962, 4579.

[18] W. R. Moore and H. Arzoumanian, *J. Org. Chem.*, 1962, **27**, 4667.

[19] G. W. K. Cavill and D. H. Solomon, *J. Chem. Soc.*, 1954, 3943.

[20] D. I. Davies, *J. Chem. Soc.*, 1963, 2351.

[21] D. F. de Tar and Chin-Chiun Chu, *J. Amer. Chem. Soc.*, 1960, **82**, 4969.

[22] L. F. Fieser, R. C. Clapp, and W. H. Daudt, *J. Amer. Chem. Soc.*, 1942, **64**, 2052.

[23] C. Graebe and C. Aubin, *Annalen*, 1888, **247**, 257.

[24] J. R. E. Hoover, A. W. Chow, R. J. Stedman, N. M. Hall, H. S. Greenberg, M. M. Dolan, and R. J. Ferlauto, *J. Medicin. Chem.*, 1964, **7**, 245.

temperature rising above 200° during the first hour.) The solid reaction product was extracted with ethanol (250 ml.) using a Soxhlet extractor. After removing the ethanol from the extract the resultant product was distilled to afford a mixture (~20 g.) of 2′-methyl-2-methoxycarbonylbiphenyl and 2,2′-dimethylbiphenyl, b. p. ~68°/0·03 mm.; and (*b*) the dimethyl ester of biphenyl-2,2′-dicarboxylic acid. Fraction (*a*) was dissolved in ethanol (50 ml.) and boiled at reflux for 6 hr. with 20% potassium hydroxide (100 ml.). After cooling the reaction mixture, 2,2′-dimethylbiphenyl was extracted with ether (3 × 50 ml.). Acidification of the alkaline solution then afforded 2′-methylbiphenyl-2-carboxylic acid (Ig) which was extracted with hot, light petroleum (b. p. 60—80°) (3 × 100 ml.) in which any contaminating biphenyl-2,2′-dicarboxylic acid (Ib) is insoluble. The crude acid was recrystallised from light petroleum (b. p. 60—80°) to afford 2′-methylbiphenyl-2-carboxylic acid as white needles (8 g.), m. p. 104—105° (lit.,[25] m. p. 104·4—105·6°).

Diacyl Peroxide of 2′-Nitrobiphenyl-2-carboxylic Acid.—2′-Nitrobiphenyl-2-carboxylic acid (Ic) (2·5 g.) was boiled at reflux with thionyl chloride (3·5 ml.) for 1·5 hr. The excess of thionyl chloride was removed *via* azeotropic distillation with anhydrous benzene and the residual crude acid chloride was dissolved in chloroform (10 ml.). Sodium peroxide (0·6 g.) was dissolved in ice-cold water (10 ml.) and the solution added to the chloroform solution of the acid chloride; the resultant mixture was stirred overnight, when the peroxide was precipitated; a further quantity was obtained on dilution of the filtrate with methanol (20 ml.) followed by ice cooling. The *diacyl peroxide* (2·2 g.), m. p. 146·5° (decomp.), was obtained as pale yellow crystals (Found: C, 63·7; H, 3·7; N, 5·9. $C_{26}H_{16}N_2O_8$ requires C, 64·45; H, 3·33; N, 5·75%).

Amounts of reactants, and yields of product 3,4-benzocoumarin (V)

2′-Substituent in acid	Acid (g.)	Lead tetra-acetate (g.)	Benzene (ml.)	Reaction time (hr.)	Recovered acid (g.)	Yields of 3,4-benzocoumarin (V) Wt. (g.)	% based on starting acid	% allowing for acid recovered
H	Ia (3)	1·67	100	24	2·27	0·64	22	89
CO_2H	Ib (19)	30	500	1	0	1·03	6·7	
NO_2	Ic (5·11)	4·54	100	96	4·09	0·15	3·6	18
Cl	Id (0·31)	0·285	100	36	0·09	0·074	28	40
OMe	Ie (2·03)	2·04	100	18	0·63	1·19	68	99
CO_2Me	If (0·51)	0·40	100	24	0·32	0·054	19	37
Me	Ig (1·15)	1·2	150	168	*	Trace	*	*

Trace = <0·5%.

* Not estimated.

Diacyl Peroxide of 2′-Chlorobiphenyl-2-carboxylic Acid.—This was similarly prepared as white crystals, m. p. 140° (75% yield), from 2′-chlorobiphenyl-2-carboxylic acid (Id). It could only be isolated from the reaction mixture on dilution with methanol (Found: C, 66·9; H, 3·4. $C_{26}H_{16}Cl_2O_4$ requires C, 67·3; H, 3·45%).

General Procedure for the Reaction of Carboxylic Acids with Lead Tetra-acetate.—The acid and lead tetra-acetate (mole ratio ~2 : 1) were dissolved in sodium-dried 'AnalaR' benzene (usually 100 ml.) and the solution heated at reflux under nitrogen until a test portion of the solution produced no blue colour with moist starch–iodide paper, indicating that reaction was complete. A white precipitate of Pb^{II} salts was always present at the end of the reaction, and ether (100 ml.) was added to help precipitate those Pb^{II} salts which have some solubility in benzene. The Pb^{II} salts were filtered off and washed with ether (50 ml.). The filtrate and ether washings were extracted with an excess of cold 0·5N-sodium hydroxide, to remove unchanged carboxylic acid, and with water. The resultant ether–benzene solution of the organic products was then concentrated and investigated by g.l.c. using column B at 125° to detect monosubstituted benzenes, and at 200° to detect 3,4-benzocoumarin (V) and other high boiling products. When 3,4-benzocoumarin was the only major organic product formed [from acids (Ia), (Ib), and (Ie)] it was isolated by evaporation of the solvent and recrystallisation from ethanol; it had m. p. 92°. The amounts of the reactants and yields of product 3,4-benzocoumarin are given in the Table. The following notes record the search for other products, and where appropriate the methods employed in their isolation.

Acid (Ib). Biphenyl is a trace product. The major product is the Pb^{II} salt of biphenyl-2,2′-dicarboxylic acid.

Acid (Ic). Nitrobenzene is a trace product; no nitrogen dioxide is evolved from the reaction. Biphenyl and 3,4-benzocoumarin (V) were detected as major organic products and were separated using thick-layer chromatography. Elution with light petroleum (b. p. 60—80°) allowed isolation of biphenyl (0·055 g.), m. p. 70°, and elution with 10% acetone in benzene a crude product showing i.r. absorptions characteristic of an aromatic nitro-group at 1525 and 1350 cm.$^{-1}$ in addition to the lactone carbonyl at 1730 cm.$^{-1}$. The position of the nitro-group absorption is similar to that of 6- and 7-nitro-3,4-benzocoumarin[26] and suggests that 5-nitro-3,4-benzocoumarin may be a reaction product. Analytical g.l.c. on column A at 210° showed the presence of a minor product with a somewhat longer retention time than 3,4-benzocoumarin (V). Purification of the crude product by vacuum sublimation gave 3,4-benzocoumarin (V) (0·15 g.), m. p. 92—92·5° as sole isolable product.

Acid (Id). In a preliminary experiment, acid (5·03 g.), lead tetra-acetate (5 g.), and benzene (150 ml.) were used to give a crude product from which the following compounds were isolated by preparative g.l.c. at 200°; biphenyl, m. p. 70°, 2-chlorobiphenyl, m. p. 32°, 3,4-benzocoumarin (V), m. p. 91—92°, and *2-chloro-o-terphenyl*, a colourless oil b. p. 120°/0·05 mm., $n_D^{19·5}$ 1·6406 (Found: C, 81·6; H, 5·05; Cl, 13·3. $C_{18}H_{13}Cl$ requires C, 81·65; H, 4·9; Cl, 13·4%). In the experiment recorded in the Table, the reaction product mixture was washed with water

---

[25] M. Orchin and E. O. Woolfolk, *J. Amer. Chem. Soc.*, 1945, **67**, 122.

[26] Hsi-Lung Pan and T. L. Fletcher, *J. Org. Chem.*, 1960, **25**, 1106.

(3 × 20 ml.); chloride ion contained in these washings was estimated as silver chloride (0·044 g.). The product benzene–ether solution was concentrated and fluorene (0·042 g.) added as a marker. Analysis using quantitative g.l.c. at 200° showed the presence of biphenyl (0·004 g.), 2-chlorobiphenyl (0·003 g.), 2-chloro-*o*-terphenyl (0·042 g.) in addition to 3,4-benzocoumarin (V) (0·074 g.).

Acid (Ie). Anisole is a trace product, but no formaldehyde was detected.

Acid (If). Analytical g.l.c. on column A at 200° indicated 3,4-benzocoumarin (V) and 2-methoxycarbonyl-*o*-terphenyl[21] as major products. Evaporation of solvents showed their combined yield as 0·126 g., and the n.m.r. spectrum that they were present in the ratio 3 : 4. Thick-layer chromatography using benzene as eluent allowed for the isolation of 3,4-benzocoumarin (V), m. p. 91—92°, and 2-methoxycarbonyl-*o*-terphenyl, m. p. 68°.

Acid (Ig). Analysis by g.l.c. showed that many products were formed in addition to 3,4-benzocoumarin (V).

o-Terphenyl-2-carboxylic acid. Acid (0·52 g.), lead tetra-acetate (0·42 g.), and benzene (100 ml.); reaction time 12 hr. Unchanged acid (0·26 g.) was recovered. Evaporation of the benzene–ether solution afforded triphenylene (VIII) (0·22 g.), m. p. 196—199° (from benzene).

Thermal Decomposition of the Diacyl Peroxide of 2′-Nitrobiphenyl-2-carboxylic Acid in Benzene.—The peroxide (1 g.) was dissolved in benzene (100 ml.) and the solution boiled at reflux under nitrogen for 3 days. The nitrogen stream was passed through saturated potassium iodide solution but no nitrogen dioxide was absorbed. 2′-Nitrobiphenyl-2-carboxylic acid was removed from the reaction mixture by extraction with cold 0·5N-sodium hydroxide. Evaporation of the benzene solution gave a crude product from which, on thick-layer chromatography, 3,4-benzocoumarin (V) (0·07 g.), m. p. 91—92° was isolated together with a few yellow crystals m. p. 204—205°, insufficient for investigation, but which were thought to be 5-nitro-3,4-benzocoumarin since the i.r. spectrum of the crude product showed aromatic nitro-group absorptions at 1350 and 1525 cm.$^{-1}$ in addition to the lactone carbonyl absorption at 1730 cm.$^{-1}$.

Thermal Decomposition of the Diacyl peroxide of 2′-Chlorobiphenyl-2-carboxylic Acid in Benzene.—A solution of the peroxide (0·05 g.) in benzene (25 ml.) was boiled at reflux for 4 days. Water (2 × 10 ml.) washings of the reaction mixture gave a positive test for chloride ion. The resulting benzene solution was washed with 0·05N-sodium hydroxide (3 × 20 ml.) to remove 2′-chlorobiphenyl-2-carboxylic acid and then qualitatively analysed using g.l.c. column A at 200° which indicated that the same products are formed, and in the same proportions as in the reaction of 2′-chlorobiphenyl-2-carboxylic acid (Id) with lead tetra-acetate.

We thank Professor D. H. Hey F.R.S. for his help and interest, and Professor C. W. Rees for helpful discussions on the reactions of 2′-nitrobiphenyl-2-carboxylic acid (Ic). We are grateful to the referees for their suggestions on the improvement of the manuscript. One of us (C. W.) thanks the S.R.C. for the award of a research studentship.

[7/289 *Received, March 9th*, 1967]